Alwadi M, Badaineh R, Alwedyan T, Gogazeh E, A Badir O. Assessment of the knowledge and practice of Jordanian family medicine practitioners regarding vitamin B12 screening for type 2 diabetes mellitus patients on metformin.Pharmacy Practice 2023 Oct-Dec;21(4):2893.

https://doi.org/10.18549/PharmPract.2023.4.2893

Original Research

Assessment of the knowledge and practice of Jordanian family medicine practitioners regarding vitamin B12 screening for type 2 diabetes mellitus patients on metformin

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Received (first version): 02-Jun-2023 Accepted: 02-May-2023 Published online: 23-Nov-2023

Abstract

Background: Metformin is one of the most important treatments for type 2 diabetes mellitus (T2DM) patients. Mostly metformin has a safe profile but, in some cases, it may cause some serious long-term hematological and neurological side effects mainly due to vitamin B12 deficiency. It is proven that there is a strong association between B12 deficiency and hematological and neurological manifestations, especially for T2DM patients on metformin. Hence, the American Diabetic Association (ADA) recommends vitamin B12 screening for those on metformin for a long duration. **Objectives:** To evaluate the knowledge and practice of family physicians among diabetic patients on metformin, and to evaluate the factors that enhance and prevent vitamin B12 screening. **Method:** A validated questionnaire was designed and distributed online for family medicine practitioners between June and September 2022. 147 family physicians participated in the study. A scoring system was used to calculate the knowledge, practice, and total scores. **Results:** The results reveal a high total knowledge score among participants about vitamin B12 manifestations and screening in T2DM patients. However, only half of the participants follow the ADA recommendations routinely (53.06) %. The total practice score is low as most participants (87.7%) answer only 9 of 18 questions correctly. Moreover, the results show that those who follow ADA recommendations routinely have better knowledge and practice scores (p-value 0.00406). **Conclusion:** More awareness about ADA recommendations and the practice of vitamin B12 screening in T2DM patients who use metformin for family physicians is required, either by encouraging them to order B12 through workshops and continuous learning programs or by the availability of tools needed to test B12.

Keywords: type 2 diabetes mellitus; metformin; vitamin B12 deficiency; family Physicians

INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent health issues in the globe.[1] Of all DM types, Type 2 Diabetes Mellitus (T2DM) is the most common.[2] According to the last report of the International Diabetes Federation (IDF), the prevalence of DM in adults is 14.8% in 2022;[3] and many previous studies conducted in Jordan assert that the prevalence of T2DM has increased over the years.[4-7]

Metformin is considered the first choice for the treatment of T2DM, and it is proven that the use of metformin for a long duration and in high doses is associated with B12 deficiency as metformin affects vitamin B12 absorption.[8-11] Several studies demonstrate that the deficiency of B12 among metformin users has expanded from 5.8% to 30% worldwide.[12-14]

Vitamin B12 deficiency is associated with many hematological and neurological consequences such as anemia, tiredness, tingling, and numbness in extremities. Hence the screening of vitamin B12 among patients on metformin is crucial.[15,16] A systematic review of DM patients on metformin encourages treating and preventing B12 deficiency to prevent neuropathy.[17] American Diabetic Association (ADA) recommends routine B12 monitoring for T2DM on metformin to prevent consequences associated with B12 deficiency, especially anemia, and neuropathy for patients on metformin for a long duration.[18]

Many DM patients are diagnosed and treated by Family physicians (FP) as they are part of the primary healthcare setting. This is referred to several reasons such as lower cost, shortage of endocrinologists, and rise in DM cases.[19] Hence, their perception and implementation of vitamin B12 screening in metformin-used T2DM patients are significant.

The primary objectives of this study are to evaluate family medicine physicians about the knowledge of vitamin B12 deficiency among T2DM patients on metformin, and their practice of screening and prescribing vitamin B12 for those patients according to ADA recommendations. The secondary objective concerns the factors that prevent and enhance screening of vitamin B12 among those physicians.

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www.pharmacypractice.org (eISSN: 1886-3655 ISSN: 1885-642X)

https://doi.org/10.18549/PharmPract.2023.4.2893

METHOD AND MATERIAL

Study design

This observational cross-sectional study, which used a self-administered questionnaire was conducted among family medicine physicians in Jordan. For this purpose, a Microsoft survey form was distributed to participants' groups through social networks between June 2022 and September 2022.

Questionnaire design

The questionnaire was designed based on a literature review and consisted of 19 questions including close-ended questions.[20] The closed-ended questions were multiple choice, categorical, dichotomous, and Likert-type questions with five-point rating scales.

It comprised three sections: The first section was dedicated to the participants' sociodemographic data and medical history. The second section retrieved information about the knowledge of family medicine physicians about B12 deficiency signs and symptoms in addition to their knowledge about the recommendation for B12 screening in T2DM on metformin. The second section was about the practice of B12 screening among family medicine physicians. The last section discusses the factors that enhance the practice.

The questionnaire was reviewed by two clinical pharmacists for structure, content validity, and applicability. In addition, a pilot test was conducted on 10 family medicine physicians (who were not included in our sample) to assess the clarity, understandability, and structure of the questionnaire, and after reviewing the feedback, the survey was further refined.

Data analysis

Survey responses were analyzed using R programming language. Results were expressed as numbers and percentages for categorical variables and as mean and standard deviation (SD) for continuous variables.

A scoring system was developed to compare the knowledge and practice of the different respondents:

- When the respondent chose the best answer to the question asked, he was granted a point.
- When the respondent chose any answer other than the best answer, he did not get a point.
- No points were taken from the respondent, he either got a point or did not.
- The questionnaire's overall score ranges from 0 (no best answers were chosen) to 33 (all best answers were chosen).
- The knowledge part of the questionnaire consists of 15 questions (ranging from 0 to 15).
- The practice part of the questionnaire consists of 18 questions (ranging from 0 to 18).

Descriptive statistics (frequency distribution) were done for the responses. In addition to exploring some factors that were associated with the final score, such as comparing the knowledge (or practice) between the respondents from different demographic groups by using the Chi-square test. A P value of < 0.05 was considered statistically significant.

Ethical approval

The research was approved by the Institutional Review Board (IRB) committee and the Deanship of Scientific Research at Al-Balqa Applied University. Informed consent was obtained from participants by completing the survey. Participants were informed that data would be dealt with in strict confidentiality and for research purposes only.

RESULTS

A total of 147 family physicians, specialists, and residents, responded to the questionnaire and participated in the study. There were 75 (51.02%) males and 72 (48.98%) females, most of whom were residents 82 (55.78%). Table 1 shows the demographic profile of the participants.

Table 1. Participants' demographic profile

Demographic variables	Option	Count	(%)
Gender	Male	75	51.02%
	Female	72	48.98%
Age	<30	43	29.25%
	30-39	70	47.62%
	40-49	15	10.2%
	>50	19	12.93%
Specialty	Resident	82	55.78%
	Specialist	43	29.25%
	Consultant	22	14.97%
Experience	<5 years	59	40.14%
	5-10	48	32.65%
	>10	40	27.21%
Facility	Primary healthcare center	15	10.2%
	Comprehensive healthcare center	79	53.74%
	Hospital	53	36.05%

(80.27%) of respondents know that most DM2 patients are using metformin. 127 (86.39%) physicians know that B12 deficiency is one of the side effects of metformin, and 20 (13.61%) don't know. On the other hand, only 18 (12.24%) think that the probability of B12 deficiency with metformin use is high, and the majority 72 (48.98%) respond with low probability. 61 (41.5%) respond that B12 deficiency happens after 5 years of using metformin. Most respondents 118 (80.27%) think testing B12 in DM2 patients on metformin is important to reduce neuropathy. About half of the participants (53.06%) always update their knowledge about American Diabetes Association (ADA) recommendations. Table 2 shows the participants' responses about the knowledge part.

According to the third part of the questionnaire; the practice part, most participants (97.96%) order a B12 test for T2DM on metformin, and (58.86%) order B12 even if the patient is asymptomatic. In addition, if the patient is on metformin for a long duration, on a high dose of metformin, or has B12

https://doi.org/10.18549/PharmPract.2023.4.2893

deficiency symptoms, the participants mostly order the B12 test; (91.16%), (61.9%) and (91.84%) respectively. Table 3 shows the results of the practice part.

Table 2. Participants' knowledge of B12 deficiency among T2DM patients using metformin

Knowledge question	Option	Count	(%)
What is the probability of T2DM patients on metformin?	High Moderate Low	118 28 1	80.27% 19.05% 0.68%
What is/are Metformin's side effects? Nausea	 Yes No	 132 15	 89.8% 10.2%
Loss of appetite	Yes No	88 59	59.86% 40.14%
Stomachache	Yes No	88 59	59.86% 40.14%
Diarrhea	Yes No	129 18	87.76% 12.24%
B12 deficiency	Yes No	127 20	86.39% 13.61%
Lactic acidosis	Yes No	79 68	53.74% 46.26%
Taste change	Yes No	27 120	18.37% 81.63%
Flu-like symptoms	Yes No	7 140	4.76% 95.24%
What is the probability of B12 deficiency among metformin users?	High Moderate Low	18 57 72	12.24% 38.78% 48.98%
What is the duration required for B12 deficiency symptoms to appear among metformin users?	<1 year 1-3 years 3-5 years >5 years	3 27 56 61	2.04% 18.37% 38.1% 41.5%
Is B12 deficiency considered a severe side effect?	Yes No I don't know	96 47 4	65.31% 31.97% 2.72%
What is the importance of B12 screening among T2DM patients on metformin?	Reduce anemia Reduce neuropathy	29 118	19.73% 80.27%
Are you staying Updated about the current ADA recommendation for B12 deficiency in T2DM using metformin?	Routinely Sometimes Never	78 68 1	53.06% 46.26% 0.68%

Table 3. Participants' practice of B12 screening and prescribing among T2DM patients using metformin

Question	Option	Count	(%)
sHave you ever ordered a B12 test for T2DM patients on metformin?	Yes No	144 3	97.96% 2.04%
Should the patient have deficiency symptoms to order a B12 test?	Symptomatic Asymptomatic Not order	58 88 1	39.46% 59.86% 0.68%
For whom you order the B12 test: Patients on metformin for a long duration	 Yes No	 134 13	 91.16% 8.84%
Patients on a high dose of metformin	Yes No	91 56	61.9% 38.1%
Routinely	Yes No	29 118	19.73% 80.27%
Patients on metformin and have B12 deficiency symptoms	Yes No	135 12	91.84% 8.16%
Elderly	Yes No	42 105	28.57% 71.43%
Do not order	No	147	100%
How often do you prescribe B12 for T2DM patients on metformin?	Routinely Lab confirmation Symptomatic Never	12 120 13 2	8.16% 81.63% 8.84% 1.36%

Table 4. Factors affect B12 screening in T2DM patients on metformin

Question	Option	Count	(%)
No tools available	Yes No	133 14	90.48% 9.52%
Patient refused	Yes No	74 73	50.34% 49.66%
Workload	Yes No	70 77	47.62% 52.38%
High test cost	Yes No	90 57	61.22% 38.78%
Lab availability	Yes No	136 11	92.52% 7.48%
Few patients	Yes No	66 81	44.9% 55.1%
High income for patients	Yes No	107 40	72.79% 27.21%
Workplace Stability	Yes No	101 46	68.71% 31.29%

Chart 1 indicates the degree the participants think they have to order a B12 test when patients have B12 deficiency symptoms. Finally, when asked about prescribing B12, 120 (81.63%) participants do that upon Lab confirmation of B12 deficiency.

In the last part of the survey, the participants were asked about factors that prevent them from B12 screening and those that enhance B12 screening. The participants think that the availability of the Lab and kit is the most important factor. Table 4 shows the result of the affecting factors.

Scoring system

Knowledge score: This is the sum of the points the respondent earned while answering the questions that assess knowledge. The score ranges from 0 to 15, a point is given to the respondent for each question answered correctly.

Histogram 1 shows, the knowledge score may be assumed to follow a normal distribution. That justifies using the mean ± standard deviation (SD) for summarizing it. The knowledge score variable follows approximately a normal distribution with a mean (8.05 ± SD of 2.16). The left line represents the center of the scale, which is the expected average assuming that the scores are normally distributed. The right line represents the

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Chart 1: The degree the participants think they have to order B12 test when patients have symptoms

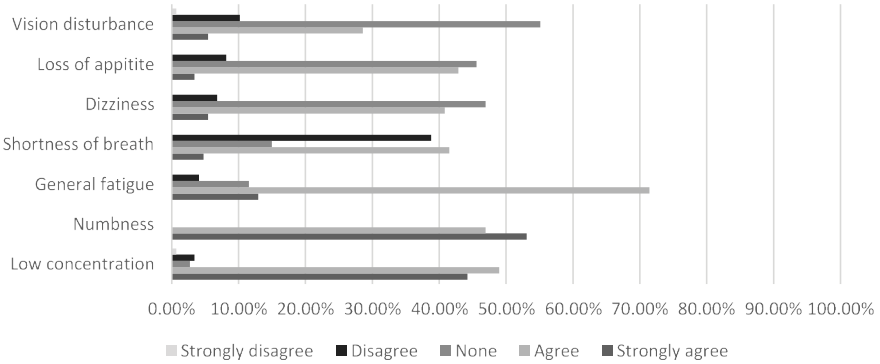
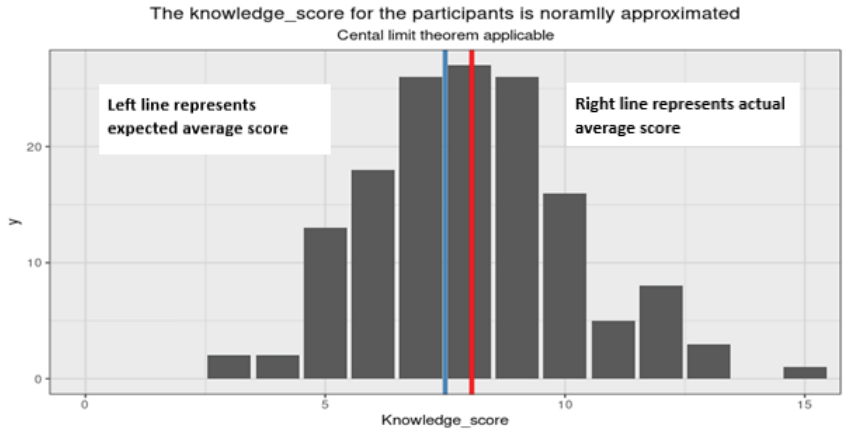


Chart 1. The degree the participants think they have to order B12 test when patients have symptoms



Histogram 1. The distribution of knowledge score

actual average score, which is higher than the statistically expected value. This positive indicator of the overall knowledge an average participant possesses.

As seen in Table 5, no participant got less than 3 marks, but only 4 out of the 147 respondents scored above 12. It may be alarming that nearly 25% of the respondents could not get at least 7 questions right (out of 15 questions). Table 5 quantifies the distribution of this variable.

Practice score: This is the sum of the points the respondent earned while answering the questions that assess practice. The score ranges from 0 to 18, a point is given to the respondent for each question that he answers correctly.

Table 5. The number of knowledge questions answered correctly

Score Group	Count	(%)
[3,6]	35	23.8%
(6,9]	79	53.7%
(9,12]	29	19.7%
(12,15]	4	2.7%

Although the knowledge score is normally approximated, the practice score is positively skewed in Histogram 2. This means that the respondents' scores on practice are below the expected average (the expected average is the center of the scale, e.g. a score of 9). The right line represents the expected average, which is the average score for a participant given that the scores are normally distributed. The left line represents the actual average, which is apparently below the expected. To sum this up, the actual practice of respondents towards B12 deficiencies in T2DM patients who take metformin is unexpectedly disappointing. Further investigations should be in order.

Compared to the distribution of the knowledge score, the scores here tend to be more negative. The fact that 87.7% of the respondents got a score of 9 or less might be alarming and require more investigations. Table 6 quantifies the distribution of this variable.

Total score: This is the sum of the points the respondent earned throughout the questionnaire. The score ranges from 0 to 33; 15 of them represent the knowledge questions and 18 of them represent the practice questions. A point is given to the respondent for each question that he answers correctly.

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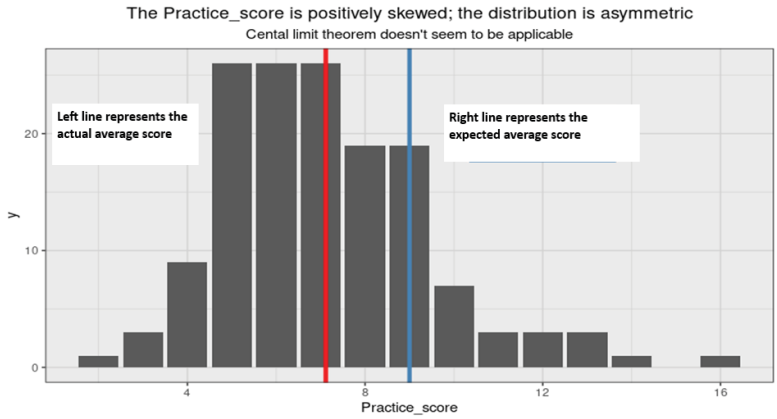

Histogram 2. The distribution of practice score

Table 6. The number of practice questions answered correctly		
Score Group	**Count**	**(%)**
[0,3]	4	2.7%
(3,6]	61	41.5%
(6,9]	64	43.5%
(9,12]	13	8.8%
[12,15]	4	2.7%
[15,18]	1	0.7%

The distribution of the total score represents the step between the encouraging results of the knowledge aspect and the disappointing results of the practice aspect. Table 7 quantifies the distribution of this variable.

Table 7. The number of knowledge and practice questions answered correctly		
Score group	Count	(%)
[5,10]	13	8.8%
(10,15]	73	49.7%
(15,20]	47	32%
(20,25]	13	8.8%
(25,30]	1	0.7%

Associations

Females, younger physicians, and less experienced physicians are better followers of the ADA recommendations. Table 8 demonstrates the association between ADA recommendations and some demographics.

A t-test comparing the average total score for the physicians who are always up-to-date with the ADA recommendations and the average for those who are only checking the ADA recommendations sometimes. Table 9 indicates that being up-to-date with the ADA recommendations and release is associated with better knowledge and practice when it comes to providing healthcare services about B12 deficiency for T2DM patients receiving metformin.

Table 8. Association between ADA recommendations and demographics			
Demographics	**Follow ADA recommendations**		**P-Value**
	Routinely	**Sometimes**	
Gender			0.002117 * *
Male	30	45	
Female	48	24	
Age			0.01732 * *
<30	31	12	
30-39	31	39	
40-49	7	8	
>50	9	10	
Experience			0.04816 **
<5	40	19	
5-10	21	28	
>10	17	22	
** P-value <0.05 is considered significant			

Table 9. Comparing the average total score for the physicians who are always up-to-date with the ADA recommendations with those who sometimes				
Statistic	**p_value**	**Estimate**	**Lower CI**	**Upper CI**
2.92	0.00406	1.77	0.571	2.97

DISCUSSION

It has been known that metformin is the cornerstone for the treatment of many T2DM patients.[21] Vitamin B12 deficiency is one of the side effects that result from metformin use and is associated with hematological and neurological complications.[22] Furthermore, a recent study has shown that metformin is accelerating the risk of autonomic neuropathy in DM patients due to B12 deficiency.[23] Therefore, prevention and treatment of vitamin B12 deficiency prevent nerve damage.[24] Family physicians were our concern in this study as they contribute widely to the treatment of T2DM patients and they should be aware of DM medication.

The recent recommendation of the ADA, in 2018, is to asses vitamin B12 levels periodically in patients who use metformin for the long term.[25] Hence, this study elucidates the knowledge and practice of family physicians regarding vitamin B12 deficiency and screening among T2DM patients on metformin. To the best of our knowledge, there is no information about Jordanian physicians' knowledge and practice regarding vitamin B12 deficiency.

The present study reveals that the respondents' knowledge score about metformin side effects and B12 deficiency and complications is high and near to optimal distribution, and this counteracts another study in the region that shows a low level of knowledge about DM treatment and medications' side effects and complications among Family physicians.[26] On the other hand, only half of the participants routinely check the updates of ADA recommendations (53.06%) associated with B12 deficiency and metformin in T2DM patients, and this comes with the results of A. Alshammari et al. in Saudi Arabia that found only 44% of physicians updated about the recent ADA guidelines for diabetics.[20] Furthermore, the study illustrates the importance of staying updated with ADA recommendations which are associated with a significantly higher total score in knowledge and practice (p-value 0.00406). Hence, this requires more awareness about the role of family physicians in T2DM management and encourages their continuous learning.

Despite having a high knowledge score, only 9 out of 18 practice questions were successfully answered by the majority of participants (87.7%), indicating a low amount of practice in vitamin B12 screening and prescribing. At the same time, most of the participants (98%) answered that they had ordered B12 tests for DM patients during their practice and this indicates that the monitoring of B12 will be easily improved among family physicians.

On the other hand, the routine monitoring and prescribing of vitamin B12 is not a common practice for T2DM patients among respondents (19.73%) and (8.16%) respectively. The same practice findings were shown in a study about vitamin B12 screening in metformin-treated diabetics in primary care, which indicates that family physicians order vitamin B12 tests only for (45%) of participants.[27] Our results emphasize the result of another study in Arab countries which states that there is a shortage in ordering serum B12 concentration in T2DM patients.[11]

Besides that, many studies highlight the limitations in B12 testing, especially with metformin users, and encourage vitamin B12 screening among physicians for those used metformin for more than 5 years.[28,29] A recent study conducted by Andrew Kien and Rehena Sultana about B12 screening and supplementation in primary care found that supplementation with B12 was associated with a lower B12 deficiency ratio (OR = 0.37) for T2DM patients who take metformin; in addition, they encourage screening of B12 for patients on 1500mg of metformin or higher and include this test in yearly check-up for DM patients.[30]

The decrease in practice level may be attributed to many reasons as the participants claimed such as the shortage of tools and the high-test cost for patients without medical assurance. This requires more attention to equipment and test kit availability through medical centers.

CONCLUSION

The study findings show that family physicians in Jordan have good knowledge about metformin and its complications. However, a large percentage do not follow ADA recommendations about vitamin B12 screening in T2DM on metformin which would affect their practice. Hence, they should be more aware of the new guidelines and recommendations, be enrolled in workshops and learning programs about DM management, and more tools and equipment for vitamin B12 screening should be available in different medical facilities.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest or financial.

ACKNOWLEDGMENTS

The authors would like to acknowledge the deanship of research at Al-Balqa Applied University for approving this study.

AUTHORS CONTRIBUTION

Maysaa Alwadi: design the study structure, collect data, write, and review the final draft. Rawan Badaineh: write, and review the final draft. Tareq Alwedyan: design the study structure, write, and collect data. Esraa Gogazeh: write, and review the final draft. Ola A Badir: write, and review the final draft.

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Assessment of the knowledge and practice of Jordanian family medicine practitioners regarding vitamin B12 screening for type 2 diabetes mellitus patients on metformin

Survey of Jordanian Family doctors

Dear Doctor,

A researcher from the specialty of Clinical Pharmacy at Al-Balqa Applied University is currently conducting a study to assess the extent of knowledge and application of family doctors to conduct vitamin B12 screening for Type II diabetes patients using metformin.

It is important to emphasize that all the information contained in this questionnaire will be treated with complete confidentiality and for research purposes only.

Participation in this study is optional and filling out the questionnaire is considered consent to participate.

Filling out the questionnaire takes about 10 minutes and your participation in this study is appreciated.

Sociodemographic part

1. Gender

- Male
- Female

2. Age

- <30
- 30-39
- 40-49
- >50

3. Specialty

- Resident
- Specialist
- Consultant

4. Experience

- <5 years
- 5-10
- >10

5. Facility

- Primary healthcare center
- Comprehensive healthcare center
- Hospital

Knowledge part

6. What is the probability of T2DM patients on metformin?

- High
- Moderate
- Low

7. What is/are Metformin's side effects? (You can choose more than one answer)

- Nausea
- Loss of appetite
- Stomachache
- Diarrhea
- B12 deficiency
- Lactic acidosis
- Taste change
- Flu-like symptoms

8. What is the probability of B12 deficiency among metformin users?

- High
- Moderate
- Low

9. What is the duration required for B12 deficiency symptoms to appear among metformin users?

- <1 year
- 1-3 years
- 3-5 years
- >5 years

10. Is B12 deficiency considered a severe side effect?

- Yes
- No
- I don't know.

11. What is the importance of B12 screening among T2DM patients on metformin?

- Reduce anemia.
- Reduce neuropathy.

12. Are you staying Updated about the current ADA recommendation for B12 deficiency in T2DM using metformin?

- Routinely
- Sometimes
- Never

Practice part

13. Have you ever ordered a B12 test for T2DM patients on metformin?

- Yes
- No

14. Should the patient have deficiency symptoms to order a B12 test?

- Symptomatic
- Asymptomatic
- Not order.

15. For whom you order the B12 test: (You can choose more than one answer)

- Patients on metformin for a long duration
- Patients on a high dose of metformin
- Routinely
- Patients on metformin and have B12 deficiency symptoms.
- Elderly
- Do not order.

16. To which degree do you think have to order a B12 test when patients have the following symptoms:

symptom	Strongly disagree	Disagree	None	Agree	Strongly agree
Low concentration					
Numbness					
General fatigue					
Shortness of breath					
Dizziness					
Loss of appetite					
Vision disturbance					

17. How often do you prescribe B12 for T2DM patients on metformin?

- Routinely
- Lab confirmation
- Symptomatic
- Never

Factors' part

18. Factors affect B12 screening in T2DM patients on metformin? (You can choose more than one answer)

- No tools available
- Patient refused.
- Workload
- High test cost
- Lab availability
- Few patients
- High income for patients
- Workplace Stability